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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,326	08/28/2003	Keith A. Hruska	JJJ-P01-599	6882

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FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
BORGEEST, CHRISTINA M	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,326	HRUSKA ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,12-17,56,57 and 69-78* is/are pending in the application.

4a) Of the above claim(s) *1-6,12-17,57 and 77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56,69-76 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/05; 2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group V, claims 56, 69-76 and 78 in the reply filed on 3 July 2006 is acknowledged. The traversal is on the ground(s) that that Groups V and Vi are have the same classification. In addition, Applicants state that Group I represents the process claims. This is not found persuasive because first, inventions in biotech are searched heavily in the non-patent literature, which is not classified. Second, issues of enablement are different with AIIRA and ACE inhibitors, and the two classes of anti-hypertensive drugs are not obvious variants. Note the article by Lewington et al. (Nephrol Dial Transplant. 2001; 16: 885-888—cited on Applicants' 1449 form filed February 2006), in which they state that "only ACE inhibitor [is] effective in reducing the inflammatory cells infiltrate...angiotensin II receptor antagonism AII [levels remain] high," thus at the time of filing, it was recognized that ACE inhibition had some advantages over AII receptor antagonism, underscoring that the two classes of drugs are not obvious variants. Third, although Group I represents the process claims, there is an extension of search and examination because issues of enablement are different for products and processes. Furthermore, the claims of Group I are not allowable at this time, thus the argument that they be rejoined upon allowance is not relevant.

In addition, Applicant has elected SEQ ID NO: 3. Claims 56, 69, and newly added claims 70-76 and 78 will be examined insomuch as they encompass a

pharmaceutical composition comprising an ACE inhibitor and a polypeptide comprising SEQ ID NO: 3.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6, 12-17, 57 and 77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or iinking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3 July 2006.

Claim Objections

Claim 78 is objected to because of the following informalities: It appears that the claim should read "A packaged pharmaceutical comprising...". Appropriate correction or clarification is required.

Information Disclosure Statement

The information disclosure statement filed 9 February 2006 contains a reference (AG) listed as U.S. Patent NO. 5,733,441 (Higley et al.), however this reference is by Chi Yin-Ko and pertains to a pre-wet filter system, thus this appears to be a typo on the IDS form. Therefore a line has been drawn through this reference. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining

compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 56 and 70-76 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sampath et al. (U.S. Patent No: 6,498,142, filed 6 May 1996) in view of London et al. (Journal of hypertension. 1996; 14: 1139-46).

The claims are drawn to a pharmaceutical composition comprising a therapeutically effective amount of an ACE inhibitor and an OP/BMP morphogen formulated with pharmaceutically acceptable salt, carrier, excipient or diluent, wherein the morphogen is the polypeptide of SEQ ID NO: 3 or wherein the morphogen is a first polypeptide including at least a C-terminal cysteine domain of a protein selected from: a pro form, a mature form, or a soluble form of a second polypeptide, wherein said second polypeptide is: OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6, or BMP9, wherein said morphogen comprises a polypeptide having at least 70% homology or 50% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP- 1, or alternatively at least 75% homology or 60% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 or alternatively, wherein said polypeptide has at least 80% homology or 70% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 or alternatively wherein said polypeptide has at least 90% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1, wherein said ACEI is: any one the compounds recited in claim 76 and a packaged pharmaceutical comprising the pharmaceutical composition of claim 56, in association with instructions for administering the composition to a mammal for treatment or prevention of chronic renal failure.

Sampath et al. teach methods and pharmaceutical preparations for use in the treatment of mammalian subjects at risk of chronic renal failure comprising administration of OP-1 formulated with appropriate excipients (as well as other BMPs

and/or OPs—see the claims; column 24, lines 30-67 and SEQ ID NO: 16 which has 100% sequence similarity with SEQ ID NO: 3 of the instant application). SEQ ID NO: 3 of the instant application encompasses the C-terminal seven cysteine domain recited in claims 71-75. Sampath et al. do not teach a pharmaceutical composition that also comprises an ACE inhibitor. London et al. teach the administration of ACE inhibitors (specifically, they administer quinapril) for renal disease. A packaged pharmaceutical is encompassed by the claims because each of the teachings suggest the administration of measured amounts of the compositions, thus encompass "packaged". Written instructions are not statutory subject matter in a patent, thus are given no patentable weight. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Sampath et al. by formulating a pharmaceutical encompassing an ACE inhibitor, as taught in London et al. because both references teach that their agents are useful to treat renal disease. The person of ordinary skill in the art would have been motivated to make the change because renal disease is known to be complicated with hypertension (see abstract of London et al.). Furthermore, the person of ordinary skill in the art could have reasonably expected success because both compositions are known in the art for treating renal disease, so the combining the compositions in one packaged pharmaceutical would have a reasonable expectation of success. Thus the claims do not contribute anything non-obvious over the prior art.

Claims 56 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sampath et al. (U.S. Patent No: 6,498,142) in view of London et al. (Journal of hypertension. 1996; 14: 1139-46) as applied to claims 56 and 70-76 and 78 in the immediately preceding paragraph and further in view of Salvetti (Drugs. 1990; 40: 800-28).

Claim 69 limits the ACE inhibitor to enalpril. Although Sampath et al. teach methods and pharmaceutical preparations for use in the treatment of mammalian subjects at risk of chronic renal failure comprising administration of OP-1 formulated with appropriate excipients and London et al. teach the administration of quinapril for renal disease, neither reference specifically teaches enalapril. Salvetti et al. review and compare the ACE inhibitors, including enalapril, thus this article suggests the similarity of action between ACE inhibitors on the market. Note especially, p. 802, whole page, which contains a discussion on the biochemistry and pharmacokinetics of ACE inhibitors. Note also, p. 802, right column, 3rd paragraph, where it is said that enalapril is more potent and has a longer duration of action. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Sampath et al. and London et al. by formulating a pharmaceutical containing the ACE inhibitor, enalapril, as taught in Salvetti, because in addition to the fact that Sampath et al. and London et al. both teach that their agents are useful to treat renal disease, Salvetti states that enalapril (recited in claim 69) is more potent and has a longer duration of action (p. 802, right column, 3rd paragraph) and additionally, Salvetti suggests the similarity of the many commercially available ACE inhibitors, thus the

knowledge of their pharmacokinetics and efficacy for reducing hypertension with many species of ACE inhibitors were well known in the art at the time of filing. The person of ordinary skill in the art would have been motivated to make the change because renal disease because of the greater potency and duration of enalapril, and for this reason as well, the person of ordinary skill in the art could have reasonably expected success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 56, 71-76 and 78 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,677,432 in view of in view of London et al. (cited above) and further in view of Vukicevic et al (J Clin Invest. 102; 1998: 202-214).

The instant claims are drawn to a pharmaceutical composition comprising a therapeutically effective amount of an ACE inhibitor and an OP/BMP morphogen formulated with pharmaceutically acceptable salt, carrier, excipient or diluent, wherein the ACE inhibitor is one of the agents recited in claim 76 and wherein the morphogen is a first polypeptide including at least a C-terminal cysteine domain of a protein selected from: a pro form, a mature form, or a soluble form of a second polypeptide, wherein said second polypeptide is: OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6, or BMP9, wherein said morphogen comprises a polypeptide having at least 70% homology or 50% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP- 1, or alternatively at least 75% homology or 60% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 or alternatively, wherein said polypeptide has at least 80% homology or 70% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1 or alternatively wherein said polypeptide has at least 90% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1, wherein said ACEI is: any one the compounds recited in claim 76 and a packaged pharmaceutical comprising the pharmaceutical composition of claim 56, in association with instructions for administering the composition to a mammal for treatment or prevention of chronic renal failure.

The claims of the '432 patent recite morphogens comprising OP-1 and/or morphogens comprising the C-terminal seven cysteine domain recited in claims 71-75. The claims of the '432 patent do not recite a pharmaceutical composition that also

comprises an ACE inhibitor, nor do they suggest the treatment of renal disease. London et al. teach the administration of ACE inhibitors for renal disease and Vukicevic teach that OP-1 administration "prevents the loss of kidney function associated with ischemic injury and may provide a basis for the treatment of acute renal failure," (see abstract)The packaged pharmaceutical (claim 78) is encompassed by the teachings because each suggest the administration of measured amounts of the compositions, thus encompass "packaged". Written instructions are not statutory subject matter in a patent, thus are given no patentable weight. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the claims of the '432 patent by formulating a pharmaceutical for the treatment of renal disease encompassing quinapril, as taught in London et al. for two reasons, 1) Vukicevic et al. strongly suggest that OP-1 could be possible for treatment for renal failure and 2) according to London et al., ACE inhibition is useful for the treatment of renal disease. The person of ordinary skill in the art would have been motivated to make the change because renal disease is known to be complicated with hypertension (see abstract of London et al.), and ACE inhibitors treat hypertension and OP-1 was already known to be useful for treatment of renal failure in mice (see abstract of Vukicevic et al.). Furthermore, the person of ordinary skill in the art could have reasonably expected success because both compositions were known in the art for their usefulness in treating renal disease, so the combining the compositions in one packaged pharmaceutical would have a reasonable expectation of success.

Claims 56 and 69 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,677,432 in view of in view of London et al. (cited above) as applied to claims 56, 71-76 and 78 in the immediately preceding paragraphs and further in view of Vukicevic et al. and Salvetti (both cited above).

Claim 69 limits the ACE inhibitor to enalpril. The claims of the '432 patent recite OP/BMP morphogens. The claims of the '432 patent do not recite a pharmaceutical composition that also comprises an enalapril, nor do they suggest the treatment of renal disease. London et al. teach the administration of ACE inhibitors for renal disease; Vukicevic teach that OP-1 administration "prevents the loss of kidney function associated with ischemic injury and may provide a basis for the treatment of acute renal failure," and Salvetti teaches the biochemistry and pharmacokinetics of ACE inhibitors on the market and that enalapril is more potent and has a longer duration of action (p. 802, right column, 3rd paragraph). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the claims of the '432 patent by formulating a pharmaceutical encompassing enalapril for three reasons, 1) Vukicevic et al. strongly suggest that OP-1 could be possible for treatment for renal failure, 2) according to London et al., ACE inhibition is useful for the treatment of renal disease and 3) according to Salvetti, enalapril is more potent and has a longer duration of action that other ACE inhibitors. The person of ordinary skill in the art would have been motivated to make the change because renal disease is known to be complicated with hypertension (see abstract of London et al.) and OP-1 was already known to be useful

for treatment of renal failure in mice (see abstract of Vukicevic et al.) and because enalapril is more potent and has a longer duration of action than other ACE inhibitors (see Salvetti, p. 802, right column, 3rd paragraph). Furthermore, the person of ordinary skill in the art could have reasonably expected success because both compositions were known in the art for their usefulness in treating renal disease, so the combining the compositions in one packaged pharmaceutical would have a reasonable expectation of success.

Claims 56, 71-76 and 78 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,846,906 in view of in view of London et al. (Journal of hypertension. 1996; 14: 1139-46) and further in view of and further in view of Vukicevic et al (J Clin Invest. 102; 1998: 202-214).The claims of the '906 patent recite morphogens comprising OP-1 and/or morphogens comprising the C-terminal seven cysteine domain recited in claims 71-75. The claims of the '906 patent do not recite a pharmaceutical composition that also comprises an ACE inhibitor, nor do they suggest the treatment of renal disease. London et al. teach the administration of ACE inhibitors for renal disease and Vukicevic et al. teach that OP-1 administration "prevents the loss of kidney function associated with ischemic injury and may provide a basis for the treatment of acute renal failure," (see abstract). The packaged pharmaceutical (claim 78) is encompassed by the teachings because each suggest the administration of measured amounts of the compositions. Written instructions are not statutory subject matter in a patent, thus are

given no patentable weight. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the claims of the '906 patent by formulating a pharmaceutical for the treatment of renal disease encompassing quinapril, as taught in London et al. for two reasons, 1) Vukicevic et al. strongly suggest that OP-1 could be possible for treatment for renal failure and 2) according to London et al., ACE inhibition is useful for the treatment of renal disease. The person of ordinary skill in the art would have been motivated to make the change because renal disease is known to be complicated with hypertension (see abstract of London et al.) and OP-1 was already known to be useful for treatment of renal failure in mice (see abstract of Vukicevic et al.). Furthermore, the person of ordinary skill in the art could have reasonably expected success because both compositions were known in the art for their usefulness in treating renal disease, so the combining the compositions in one packaged pharmaceutical would have a reasonable expectation of success.

Claims 56 and 69 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,846,906 in view of in view of London et al. (cited above) as applied to claims 56, 71-76 and 78 in the immediately preceding paragraphs and further in view of Vukicevic et al. and Salvetti (both cited above).

Claim 69 limits the ACE inhibitor to enalpril. The claims of the '906 patent recite BMP/OP morphogens. The claims of the '906 patent do not recite a pharmaceutical composition that also comprises an enalapril, nor do they suggest the treatment of renal disease. London et al. teach the administration of ACE inhibitors for renal disease;

Vukicevic teach that OP-1 administration "prevents the loss of kidney function associated with ischemic injury and may provide a basis for the treatment of acute renal failure," and Salvetti teaches the biochemistry and pharmacokinetics of ACE inhibitors on the market and that enalapril is more potent and has a longer duration of action (p. 802, right column, 3rd paragraph). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the claims of the '906 patent by formulating a pharmaceutical for the treatment of renal disease encompassing enalapril for three reasons, 1) Vukicevic et al. strongly suggest that OP-1 could be possible for treatment for renal failure and 2) according to London et al., ACE inhibition is useful for the treatment of renal disease 3) according to Salvetti, enalapril is more potent and has a longer duration of action that other ACE inhibitors. The person of ordinary skill in the art would have been motivated to make the changes because renal disease is known to be complicated with hypertension (see abstract of London et al.) and OP-1 was already known to be useful for treatment of renal failure in mice (see abstract of Vukicevic et al.) and because enalapril is more potent and has a longer duration of action than other ACE inhibitors (see Salvetti, p. 802, right column, 3rd paragraph). Furthermore, the person of ordinary skill in the art could have reasonably expected success because both compositions were known in the art for their usefulness in treating renal disease, so the combining the compositions in one packaged pharmaceutical would have a reasonable expectation of success.

Claims 56, 71-76 and 78 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 16-18 of copending Application No. 10/816,768 in view of in view of London et al. (Journal of hypertension. 1996; 14: 1139-46) and further in view of and further in view of Vukicevic et al (cited above).

The claims of the '768 application recite morphogens comprising OP-1 and/or morphogens comprising the C-terminal seven cysteine domain recited in claims 71-75. The claims of the '768 application do not recite a pharmaceutical composition that also comprises an ACE inhibitor, nor do they suggest the treatment of renal disease. London et al. teach the administration of ACE inhibitors for renal disease and Vukicevic et al. teach that OP-1 administration "prevents the loss of kidney function associated with ischemic injury and may provide a basis for the treatment of acute renal failure," (see abstract). The packaged pharmaceutical (claim 78) is encompassed by the teachings because each suggest the administration of measured amounts of the compositions. Written instructions are not statutory subject matter in a patent, thus are given no patentable weight. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the claims of the '768 application by formulating a pharmaceutical for the treatment of renal disease encompassing quinapril, as taught in London et al. for two reasons, 1) Vukicevic et al. strongly suggest that OP-1 could be possible for treatment for renal failure and 2) according to London et al., ACE inhibition is useful for the treatment of renal disease. The person of ordinary skill in the art would have been motivated to make the change because renal disease is

known to be complicated with hypertension (see abstract of London et al.) and OP-1 was already known to be useful for treatment of renal failure in mice (see abstract of Vukicevic et al.). Furthermore, the person of ordinary skill in the art could have reasonably expected success because both compositions were known in the art for their usefulness in treating renal disease, so the combining the compositions in one packaged pharmaceutical would have a reasonable expectation of success.

This is a provisional obviousness-type double patenting rejection.

Claim 56 and 69 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 16-18 of copending Application No. 10/816,768 in view of in view of London et al. (cited above) as applied to claims 56, 71-76 and 78 in the immediately preceding paragraphs and further in view of Vukicevic et al. and Salvetti (both cited above).

Claim 69 limits the ACE inhibitor to enalpril. The claims of the '768 application recite BMP/OP morphogens. The claims of the '768 application do not recite a pharmaceutical composition that also comprises an enalapril, nor do they suggest the treatment of renal disease. London et al. teach the administration of ACE inhibitors for renal disease; Vukicevic teach that OP-1 administration "prevents the loss of kidney function associated with ischemic injury and may provide a basis for the treatment of acute renal failure," and Salvetti teaches the biochemistry and pharmacokinetics of ACE inhibitors on the market and that enalapril is more potent and has a longer duration of action (p. 802, right column, 3rd paragraph). It would have been obvious to the person

of ordinary skill in the art at the time the invention was made to modify the claims of the '768 application by formulating a pharmaceutical for the treatment of renal disease encompassing enalapril for three reasons, 1) Vukicevic et al. strongly suggest that OP-1 could be possible for treatment for renal failure and 2) according to London et al., ACE inhibition is useful for the treatment of renal disease 3) according to Salvetti, enalapril is more potent and has a longer duration of action that other ACE inhibitors. The person of ordinary skill in the art would have been motivated to make the changes because renal disease is known to be complicated with hypertension (see abstract of London et al.) and OP-1 was already known to be useful for treatment of renal failure in mice (see abstract of Vukicevic et al.) and because enalapril is more potent and has a longer duration of action than other ACE inhibitors (see Salvetti, p. 802, right column, 3rd paragraph). Furthermore, the person of ordinary skill in the art could have reasonably expected success because both compositions were known in the art for their usefulness in treating renal disease, so the combining the compositions in one packaged pharmaceutical would have a reasonable expectation of success.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Claim language reciting to OP and/or BMP morphogens is

known. For example, see: US 7060680 B2, US 7056882 B2, US 6723698 B2, US 6531445 B1 and US 6399569 B1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth C. Kemmerer

Christina Borgeest, Ph.D.

ELIZABETH KEMMERER
PRIMARY EXAMINER